



COMMENT ON EDELMAN AND POLONSKY

## Type 2 Diabetes in the Real World: The Elusive Nature of Glycemic Control.

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Edelman and Polonsky (1) suggest that poor adherence to pharmacotherapy is largely (~75%) responsible for the gap between clinical efficacy from randomized controlled trials and real-world effectiveness of antihyperglycemic drugs. As no single strategy can be applied successfully to all patients with type 2 diabetes in order to improve medication adherence, other approaches are suggested, including innovation in delivery methods and reduction of the number of daily pills, shared strategies between clinicians and patients, and easier access to medications.

Only 11 years ago, the first newer diabetes drug (sitagliptin) was considered innovative for the time (once-daily administration, lower risk of hypoglycemia, and similar HbA<sub>1c</sub> reduction compared with older drugs). Moreover, the consolidated suggestion by the American Diabetes Association (ADA) to approach diabetes therapy on a personalized basis remains apparently unsuccessful, given that the proportion of patients with diabetes who achieve an HbA<sub>1c</sub> target of <7% (<53 mmol/mol) is still around 50%, with no appreciable change over the last decade. Finally, facilitated access to diabetes medications must await the time needed for newer diabetes drugs to become generic, as the global sales for

antidiabetes drugs will be \$95–110 billion in 2021 (2).

We suspect that poor adherence to pharmacotherapy is also linked to a more generalized clinical (therapeutic) inertia of clinicians (3), who may be dissatisfied about some dissonance among therapeutic guidelines released by scientific associations. Take, for example, the reputed scientific guidelines about diabetes treatment released by the ADA, the American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), and the American College of Physicians (ACP) in 2017. For ADA (4), the choice of the second drug after metformin failure should be made after careful consideration of many factors, including efficacy, adverse effects (hypoglycemia and weight change), and cost; for AACE and ACE (5), there is a hierarchy of choices after metformin failure, with preference given to newer drugs (glucagon-like peptide 1 receptor agonists and sodium-glucose cotransporter 2 inhibitors); for ACP (6), the evidence is weak for recommending any particular oral drug to add to metformin, and clinicians and patients must be allied to select among medications after discussing benefits, adverse effects, and costs. This may generate a sense of frustration among clinicians, who may perceive that the

choice of a second drug after metformin failure has marginal importance, especially in light of the residual vascular risk that remains high after intensive glycemic control.

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